NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

TEVA NEUROSCIENCE, INC., TEVA PHARMACEUTICALS USA, INC., and TEVA PHARMACEUTICALS INDUSTRIES, LTD., Plaintiffs, v. WATSON LABORATORIES, INC., MYLAN PHARMACEUTICALS, INC., MYLAN INC., ORCHID CHEMICALS & PHARMACEUTICALS LTD., ORCHID HEALTHCARE (a division of Orchid Chemicals & Pharmaceuticals Ltd.) and ORGENUS PHARMA INC. Defendants.	:	Civil Action No. 2:10-cv-05078 Opinion
TEVA NEUROSCIENCE, INC., TEVA PHARMACEUTICALS USA, INC., and TEVA PHARMACEUTICALS INDUSTRIES, LTD., Plaintiffs, v. APOTEX CORP. and APOTEX INC. Defendants.	:	Civil Action No. 2:11-cv-3076

Claire C. Cecchi, U.S.D.J.

This matter comes before the Court by request of Teva Neuroscience, Inc., Teva Pharmaceuticals USA, Inc. and Teva Pharmaceuticals Industries, Ltd. (collectively, "Teva"), Orchid,[1] Watson,[2] Mylan[3] and Apotex[4] (collectively, "Defendants") for claim construction, pursuant to Local Patent Rule 4.5. The parties sought the Court's interpretation of disputed terms in United States Patent No. 5,453,446 ("the '446 Patent"). A Markman hearing was held on January 29, 2013, at which the parties presented their arguments. Having considered the parties' written and oral arguments, the Court sets forth its construction of the disputed terms below.

Factual Background

United States Patent No. 5,453,446 claims a method of treating a patient with Parkinson's disease by administering to the patient an effective amount of a particular compound, R(+)-N-propargyl-1-amnioindan ("R(+)-PAI"). Parkinson's disease was first identified by Dr. James Parkinson in 1817. (Ruffolo Decl. ¶ 39.) The disease is "considered to be the result of degradation of the pre-synaptic dopaminergic neurons in the brain, with a subsequent decrease in the amount of the neurotransmitter dopamine, that is being released." ('446 Patent, 1:27-30.) This inadequate release of dopamine "leads to the onset of voluntary muscle control disturbances symptomatic of Parkinson's disease." (Id., 1:30-33.) At the time of application, various procedures for treating Parkinson's disease existed, such as Levodopa ("L-Dopa") treatment. (Id., 1:34-37.) L-Dopa, a dopamine precursor, is "converted into dopamine resulting in increased

[1] "Orchid" consists of Orchid Chemicals & Pharmaceuticals Ltd., Orchid Healthcare (a division of Orchid Chemicals & Pharmaceuticals Ltd.) and Orgenus Pharma Inc.
[2] "Watson" consists of Watson Pharma and Watson Laboratories, Inc.
[3] "Mylan" consists of Mylan Pharmaceuticals, Inc., Mylan Inc. and Mylan LLC.

levels of dopamine" in dopaminergic neurons. (Id., 1:42-44.) However, L-Dopa treatment had certain drawbacks, including diminished clinical response after the first few years of treatment. (Id., 1:49-51.)

In order to overcome these effects, L-Dopa was administered with drugs called MAO inhibitors. (Id., 1:66-2:3.) MAO exists in two forms – MAO-A and MAO-B – which have selectivity for different substrates and inhibitors. (Id., 2:4-5.) MAO-B is an enzyme involved in the breakdown of dopamine in the brain. A drug that inhibits MAO-B will therefore prevent the breakdown of dopamine that is produced, resulting in increased levels of dopamine in the brain. (Ruffolo Decl. ¶¶ 63,64.) One MAO-B inhibitor in particular, (-)-deprenyl, had been extensively studied and used in conjunction with L-Dopa treatment. ('446 Patent, 2:25-27.) Unfortunately, (-)-deprenyl was not without its own adverse side effects. (Id., 2:42-43.)

As a result, other MAO-B inhibitors free of the undesirable effects associated with (-)-deprenyl were investigated. (Id., 2:52-54.) One such compound was N-propargyl-1-amnioindan (known as "AGN-1135" or "PAI"). PAI is a "potent, selective irreversible inhibitor of MAO-B . . .[that] does not give rise to unwanted sympathomimetic effects." (Id., 2:57-58.) PAI is compound that contains equal amounts of two enantiomers, also referred to as a "racemic mixture" or racemate. (Ruffolo Decl. ¶ 34.)

"Molecules that have the same chemical substituents, but different spatial arrangements, are referred to as stereoisomers." Sanofi-Synthelabo v. Apotex, Inc., 470 F.3d 1368, 1372 (Fed. Cir. 2006). "Enantiomers are a pair of stereoisomers that are non-superimposable mirror images of each other." Pfizer, Inc. v. Ranbaxy Labs. Ltd., 457 F.3d 1284, 1286 (Fed. Cir. 2006). This

[4] "Apotex" consists of Apotex Corp. and Apotex Inc.

characteristic is "often likened to the relative structures of a person's right and left hands." Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713, 720 (N.D.W.Va. 2004). Enantiomers are capable of rotating plane-polarized light; enantiomers that rotate polarized light to the right are referred to as (+); enantiomers rotating polarized light to the left are referred to as (-). Id. at 720-21; Sanofi-Synthelabo, 470 F.3d at 1372. Enantiomers are also sometimes designated d- (dextrorotatory or right rotating) or l- (levorotatory or left rotating), again referring to the direction of optical rotation. Id. "Chemists also distinguish between enantiomers by designating an enantiomer as either 'R' or 'S' based upon the arrangement of certain atoms at the enantiomer's 'chiral center.' Where one enantiomer is an 'R,' the other will be an 'S.'" Ortho-McNeil, 348 F. Supp. 2d at 720- 21.

Because "deprenyl has a similar structure to PAI, and it is known that the (-)-enantiomer of deprenyl, i.e. (-)-deprenyl, is considerably more pharmaceutically active than the (+)-enantiomer, it was expected, by those skilled in the art, that only the (-)enantiomer of PAI would be the active MAO-B inhibitor." (Id., 3:12-17.) However, "contrary to such expectations," the inventors of the '446 Patent discovered that "the (+)-PAI enantiomer was in fact the active MAO-B inhibitor while the (-)enantiomer showed extremely low MAO-B inhibitory activity." (Id., 3:18-22.) Furthermore, R(+)-PAI "surprisingly also had a higher degree of selectivity for MAO-B inhibition than the corresponding racemic form." (Id., 3:22-25.) Finally, "it was shown that (+)PAI ha[d] the R absolute configuration." (Id., 3:29-30.) As such, the invention claimed by the '446 Patent is the treatment of Parkinson's disease with an effective amount of R(+)-N-propargyl-1-aminoindan, or R(+)-PAI.

Procedural Background

On October 1, 2010, Teva filed suit against Watson, Mylan and Orchid for infringement of the '446 Patent based on their submissions of Abbreviated New Drug Applications ("ANDAs") seeking approval to sell generic versions of Azilect® (rasagiline tablets). Azilect® is the trade name for Teva's Parkinson's disease drug. The '446 Patent is listed in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book") in connection with Azilect®. On May 27, 2011, Teva filed suit against Apotex based on Apotex's filing of its own ANDA. All Defendants filed their ANDAs prior to the expiration of the '446 Patent. The lawsuits were consolidated on October 28, 2011. Defendants deny Teva's allegations of infringement and instead argue that the '446 patent is invalid, unenforceable and/or not infringed.

The relevant claims for the Court's consideration are Claims 1 and 17.[5] Claim 1 states: "A method of treating a subject for Parkinson's disease which comprises administering to the subject an amount of R(+)-N-propargyl-1-aminoindan or a pharmaceutically acceptable salt thereof effective to treat the subject." ('446 Patent, 20.) Claim 17 states: "The method of claim 1 which further comprises administering to the subject Levodopa in an amount relative to the amount of R(+)-N-propargyl-1-aminoindan or a pharmaceutically acceptable salt thereof

[5] Claim 18 states: "The method of claim 1 which further comprises administering to the subject a decarboxylase inhibitor in an amount effective to ensure L-Dopa uptake." ('446 patent, 22.) Although the Majority Defendants initially disputed this term, it appears that the parties are now in agreement that this term should be construed as follows: "[a]n amount of the decarboxylase inhibitor which is sufficient to inhibit peripheral metabolism of L-Dopa and therefore allow L-Dopa uptake in the brain." (See Majority Defendants' Opening Claim Construction Brief 34.)

effective to treat the disease." ('446 Patent, 21.) In particular, there are five claim terms for the Court to construe. These terms are: "R(+)-N-propargyl-1-aminoindan" (Claims 1, 17); "treating a subject for Parkinson's disease" and "effective to treat the subject" (Claim 1); "comprises" (Claims 1, 17); and "in an amount relative to the amount of" (Claim 17).

Legal Standard

Claim construction is a matter of law to be determined by the Court. Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005), cert. denied, 546 U.S. 1170 (2006). To construe the terms of a patent, a Court should look first to the language of the claim itself. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). Terms within a claim "are generally given their ordinary and customary meaning." Id. Specifically, "the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art ("POSA") in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1313.

In order to determine how a POSA would understand a patent's claim language, the Court must first look to the intrinsic record—the patent itself, including the claims, the specification and the prosecution history. Vitronics, 90 F.3d at 1582 (citing Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996)). The specification "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Id. The Federal Circuit has explained that the specification is "usually . . . dispositive . . . [and is the] best guide to the meaning of a disputed term." Phillips, 415 F.3d at 1315 (quoting Vitronics, 90 F.3d at 1582) (internal quotations omitted). It is therefore proper for a court to "rely heavily on the written description for

guidance as to the meaning of the claims." Id. at 1317.

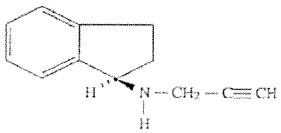
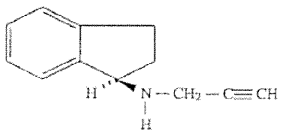
A patent's prosecution history is also an important source to consider, as it "provides evidence of how the [Patent Trademark Office] and the inventor understood the patent." Id. Further, the prosecution history "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id. As such, the Federal Circuit has emphasized the need to consult the prosecution history in order to "exclude any interpretation that was disclaimed during prosecution." See Rhodia Chimie v. PPG Indus., 402 F.3d 1371, 1384 (Fed. Cir. 2005).

After consulting the intrinsic evidence, a Court may then examine the extrinsic evidence, or "all evidence external to the patent and prosecution history." Markman, 52 F.3d at 980; Phillips, 415 F.3d at 1317-18 (stating that the Federal Circuit "ha[s] authorized district courts to rely on extrinsic evidence"). Extrinsic evidence includes testimony by the inventor or by experts, dictionaries, and treatises. Markman, 52 F.3d at 980. However, extrinsic evidence is generally "less significant than the intrinsic record in determining the legally operative meaning of claim language." C.R. Bard. Inc. v. U.S. Surgical Corp., 388 F.3d 858, 862 (Fed. Cir. 2004) (quotations omitted). Moreover, when relied upon, extrinsic evidence must be considered in view of the specification and prosecution history. Phillips, 415 F.3d at 1320. ("[E]xtrinsic evidence may be useful to the court, but it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of intrinsic evidence.").

Discussion

A. "R(+)-N-propargyl-1-aminoindan"

The parties dispute the construction of this term, which appears in Claims 1 and 17. The parties' proposed constructions are:

	Teva's Construction	**Orchid's/Watson's Construction**	**Mylan's Construction**	**Apotex's Construction**
R(+)-N-propargyl-1-aminoindan	A compound containing the optically active enantiomer rotating plane-polarized light in a clockwise direction and having an R absolute stereochemical configuration of the following chemical structure:  The compound is now known as rasagiline. It is at least substantially pure and may include small amounts of the other enantiomer.	A compound containing the optically active enantiomer rotating plane-polarized light in a clockwise direction and having an R absolute stereochemical configuration of the following chemical structure:  The compound is now known as rasagiline.	Pure R(+)-N-propargyl-1- aminoindan without the presence of any amount of the S(-) enantiomer.	Rasagiline.

Therefore, the question with regard to this term is whether the construction should include an enantiomeric purity limitation, and if so, what purity level is required.

Teva argues that a POSA would understand that R(+)-PAI, as used in the claims, must be at least substantially pure in order to achieve the objective of the '446 Patent and to distinguish the claimed compound from the prior art. At the same time, Teva argues that R(+)-PAI may

include small amounts of the other enantiomer because 100% purity would not have been a realistic or practical achievement using the resolution methods discussed in the '446 Patent. Orchid, Watson and Apotex (the "Majority Defendants") would construe this term as written, i.e. without a specific purity level. Mylan, on the other hand, takes the view that the term requires absolute purity of R(+)-PAI without the presence of *any* of the corresponding S(-) enantiomer.

The Court agrees with Teva. Looking first at the plain language, the claims at issue expressly require the R(+) enantiomer of PAI. As such, a POSA at the time of the invention would understand that the "R(+)" denotes that a compound has some level of enantiomeric purity. See Markman v. Westview Instruments, Inc., 52 F.3d 967, 986 (Fed. Cir. 1995) (explaining that a court is required to give each disputed claim term the meaning it would have had to "one of ordinary skill in the art at the time of the invention"); Ortho-McNeil Pharm., Inc. v. Mylan Laboratories, Inc., 348 F.Supp. 2d 713, 730 (N.D.W.Va. 2004), aff'd without opinion, 161 Fed. Appx. 944 (Fed. Cir. 2005) (holding that a POSA would necessarily understand a claim to S(-) ofloxacin ("levofloxacin") to be "substantially pure"). Because the Majority Defendants' construction could essentially allow for a compound that contained substantial amounts of the S(-) enantiomer, so long as it contained at least 51% of the R(+) enantiomer, the proposed construction would not comport with a POSA's understanding of the claims at the time of the invention. (See Majority Defendants' Opening Claim Construction Brief 11-12) ("The bottom line is that if the amount of R(+) N-propargyl-1-aminoindan rotates light in a clockwise fashion to a *measureable* degree, it is the R(+) enantiomer") (emphasis added).

In addition, construing the term to cover a compound that closely resembles the racemic mixture – rather than a substantially pure compound – would negate the stated objective of the

invention, which was to prepare and use a "novel" compound, R(+)-PAI. ('446 Patent, Abstract.) Indeed, the specification of the '446 Patent clearly distinguishes between R(+)-PAI and the racemic mixture from which R(+)-PAI was derived. The invention is described as "relat[ing] to the R(+) enantiomer of N-propargyl-1-aminoindan . . . which is a selective irreversible inhibitor of the B-form of the monoamine oxidase enzyme." ('446 Patent, 1:15-18.) The specification goes on to state that one object of the invention is to "separate the racemic PAI compounds and produce an enantiomer with MAO-B inhibition activity." (Id., 3:8-10.) Both the detailed description of the invention and the examples teach the use of well-known separation methods for preparing R(+)-PAI from the racemic mixture. (Id., 4:36-49, 5:19-21; see examples 2-3, 7:19-45.)

Similarly, the specification's focus not only on the differences between R(+)-PAI and the racemic compound, but also between R(+)-PAI and S(-)-PAI, further demonstrates that R(+)-PAI must be "substantially pure." Example 19 of the '446 Patent compared the "[i]nhibitory activity of the R(+)-PAI, S(–)-PAI and racemic PAI." ('446 Patent, 11:53-54.) The results of the example showed that R(+)-PAI was "twice as active as the racemate for inhibition of MAO-B." (Id., 11:60-62.) More interestingly, S(-)-PAI was "only 1/6,800 as active as the R(+)-PAI for inhibition of MAO-B." (Id., 11:66-67.) In other words, the extremely high MAO-B inhibitory activity of R(+)-PAI, as compared to the corresponding S(-)-PAI, indicates that the R(+)-PAI disclosed in the patent cannot resemble the racemic mixture. Instead, R(+)-PAI must be *close* to enantiomerically pure. A construction of R(+)-PAI that may encompass the racemic compound, or something very similar to it, would therefore negate the explicit teachings of the patent.

Notably, however, the specification does not disclose that R(+)-PAI must be 100%

enantiomerically pure, as Mylan argues. Indeed, even the Majority Defendants agree that the R(+)-PAI produced in examples 3, 4 and 6 would not be 100% enantiomerically pure. (Majority Defendants' Opening Claim Construction Brief 12-13). Mylan has not sufficiently cast doubt on Teva's *and* the Majority Defendants' position that, based on a POSA's understanding at the time of the invention, use of the purification methods described in the '446 Patent would yield a product that was less than 100% pure. As such, Mylan's proposed construction is without merit. Simply put, a plain reading of the specification leads to the conclusion that the compound claimed is of substantial enantiomeric purity, but not necessarily a compound completely devoid of even a single S(-) enantiomer.

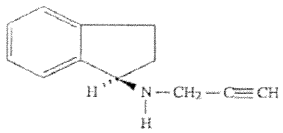
Although the intrinsic evidence is sufficient to support the Court's construction, the Court finds that the extrinsic evidence also indicates that a POSA would understand the term R(+) PAI to mean a compound that is substantially pure, but not one that requires the complete absence of the S(-) enantiomer. Plaintiffs' expert, Dr. Ruffolo, explains that "the extremely high MAO-B inhibition activity disclosed for R(+)-PAI in the '446 Patent compared to that of S(-)PAI (up to 6,800-fold), could only be achieved by substantially pure R(+)-PAI." (Ruffolo Dec. ¶ 57.) Similarly, "a POSA would understand that once R(+) PAI had been chosen to use as a treatment, it would be substantially enantiomerically pure, with only small quantities of the S(-) enantiomer present." (Id.) In terms of 100% purity, Dr. Ruffolo indicates that based on the enantiomer separation methods referenced in the '446 Patent, a "POSA would have . . . known that absolute enantiomeric purity (i.e., 100% optical purity) was not achievable using the conventional optical separation methods to produce an individual enantiomer from a racemic mixture." (Ruffolo Decl. at ¶ 56.) "Because those methods have inherent limitations, even repeated purification

efforts cannot completely exclude every molecule of the other enantiomer." (Id.) As such, Dr. Ruffolo argues that "absolute (100%) purity is not attainable as a practical matter." (Id.) Defendants' argument to the contrary does not sufficiently instruct the Court on the central issue of how a POSA – at that time *and* in light of the teachings of the '446 Patent – would have understood R(+)-PAI in terms of its enantiomeric purity. Therefore, the Court adopts Teva's proposed construction of this term.

Finally, another patent case involving the use of an enantiomer in a method of treatment claim is instructive. See Ortho-McNeil, Inc., et. al v. Johnson & Johnson Pharma. Res. & Dev., LLC, et. al, 348 F.Supp. 2d 713 (N.D.W.Va. 2004). There, similar to this case, the claims did not "expressly refer to a specific minimum optical purity." Id. at 730. However, the Court construed the relevant term to be "substantially pure levofloxacin." In doing so, the Court explained that "[a]lthough one of ordinary skill in the art would have understood the claim to the compound levofloxacin to be *substantially pure* levofloxacin, the realities of science would have led such a skilled artisan to conclude that purity was not 100 percent." Id. (emphasis added) As here, the Court cited to the specification and the examples to support its construction.

Accordingly, the Court construes R(+)-N-propargyl-1- aminoindan as:

"A compound containing the optically active enantiomer rotating plane-polarized light in a clockwise direction and having an R absolute stereochemical configuration of the following chemical structure:



The compound is now known as rasagiline. It is at least substantially pure and may include small amounts of the other enantiomer."

B. "treating a subject for Parkinson's disease" and "effective to treat the subject"

The parties dispute the construction of this term, which appears in Claim 1. The parties' proposed constructions are:

	Teva's Construction	**Orchid's/Watson's/ Apotex's Construction**	**Mylan's Construction**
treating a subject for Parkinson's disease…effective to treat the subject	effecting some alleviation in one or more of the symptoms of Parkinson's disease	treating the pathological features of Parkinson's disease, e.g. damage to nigrostriatal dopaminergic neurons, in a subject by slowing or stopping the progression of the disease	no construction necessary

The question for the Court is whether "treatment" refers to treating the symptoms of Parkinson's disease, or in the alternative, to treating the actual neurodegeneration caused by the disease.

The specification of the '446 Patent makes clear that the invention involves treatment of the symptomatic, rather than the pathological features, of Parkinson's disease. For example, the '446 Patent explains that a "decrease in the amount of the neurotransmitter dopamine . . . leads to the onset of voluntary muscle control disturbances *symptomatic* of Parkinson's disease." ('446 Patent, 1:27-33) (emphasis added.) The specification goes on to explain that various procedures for treating Parkinson's disease have been established, including treatment with L-Dopa. (Id., 1:34-49.) Administration of L-Dopa results in increased levels of dopamine in dopaminergic neurons, thereby "alleviat[ing] the *symptoms* of the disease and contribut[ing] to the well-being of the patients." (Id., emphasis added.) The patent also explains that the addition of a MAO-B inhibitor, i.e. (-)-deprenyl, to L-Dopa treatment leads to symptomatic improvements "in akinesia

and overall functional capacity." (Id., 2:25-37; Ruffolo Decl. ¶¶ 63,64.) Because R(+)-PAI is also a MAO-B inhibitor (see id., examples 21 and 25), a POSA would reasonably conclude that "treatment" with R(+)-PAI would similarly result in improvements in the *symptoms* caused by Parkinson's disease. (Id., example 24, 16:67-17:2) (explaining that "R(+)-PAI is an excellent MAO-B inhibitor in vivo, and is of especially great potential for the treatment of Parkinson's disease.") In other words, a POSA would understand that MAO-B inhibition by R(+)-PAI would increase dopamine levels in the same way as MAO-B inhibition by (-)-deprenyl, thereby alleviating the symptoms of Parkinson's disease.

The testimony of Plaintiff's expert Dr. Ruffolo further supports the Court's finding that "treatment" as used in the claims of the '446 patent refers to treatment of the symptoms caused by Parkinson's disease. Dr. Ruffolo testified that the patent's disclosure "supports the conclusion that a POSA would have understood that treatment of Parkinson's disease with R(+)-PAI would alleviate voluntary muscle control symptoms associated with Parkinson's disease because of its direct effect as a MAO-B inhibitor that would result in increased brain dopamine levels that would alleviate symptoms." (Ruffolo Decl. ¶ 71.) Additionally, Dr. Ruffolo explained that a POSA would necessarily understand "treatment" to mean alleviation of symptoms because "[t]he cause of death of the dopaminergic neurons leading to Parkinson's disease. . . was not known [as of 1990] and, is still not known today." (Ruffolo Decl. ¶ 40.) As such, "[t]reatment focused on alleviating symptoms of the disease by using drugs that increase dopamine levels in the brain or in some other way increase dopamine transmission." (Id.)

The Majority Defendants rely on data from example 24 to argue that treatment of the pathological features of Parkinson's disease is an essential objective of the invention. However,

the Majority Defendants' reliance on example 24 to support their proposed construction is misplaced. Example 24 expresses only the *hope* that R(+)-PAI could neutralize the damaging effects of MPTP, a neurotoxin, *if* in fact MPTP or another environmental toxin was the cause of Parkinson's disease. Example 24 states:

> One of the major current *hypotheses* suggests that the progressive nigrostiatal degeneration in Parkinson's *may be due* to the exposure to environmentally-derived exogenous MPTP-like neurotoxins. In such case, there is an additional strong indication to initiation of sustained treatment with an MAO-B inhibitor from the very early stages of Parkinson's disease in the *hope* that it will neutralize the damaging effects of such yet *putative* MPTP-like toxins and thus arrest or slow down the progression of the illness.

('446 Patent, 16:4-13) (emphasis added.) This speculative conclusion regarding the possibility of neuroprotection by R(+)-PAI is insufficient to warrant a construction of "treatment" that is restricted to only pathological features. See Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 909 (Fed. Cir. 2004) (explaining that "absent a clear disclaimer of particular subject matter, the fact that the inventor may have anticipated that the invention would be used in a particular way does not mean that the scope of the invention is limited to that context"). This is especially true where other references in specification point to *symptomatic* treatment of Parkinson's disease through the administration of MAO-B inhibitors and L-Dopa.

As such, the Court construes "treating a subject for Parkinson's disease" and "effective to treat the subject" as "effecting some alleviation in one or more of the symptoms of Parkinson's disease."

C. "comprises"

Only Mylan disputes the construction of the term "comprises," which appears in Claims 1 and 17:

	Teva's/Orchid's/Watson's/Apotex's Construction	**Mylan's construction**
comprises	allows additional unrecited method steps to be performed including the co-administration of other therapies for Parkinson's disease	allows additional method steps including co-administration of other drugs, but does not allow the administration of any enantiomer of PAI other than the R enantiomer and does not allow for administration of drugs to treat diseases other than Parkinson's disease

As to the first part of Mylan's proposed construction, the Court has already found, in connection with the construction of R(+)-PAI, that the compound is at least substantially pure and may include small amounts of the other enantiomer. In other words, the methods of Claims 1 and 17 *would* allow for the administration of small amounts of the S enantiomer.

In addition, the Federal Circuit has held that "comprising" is "a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501 (Fed. Cir. 1997); Amgen Inc. v. Hoechst Marion Roussel, 314 F.3d 1313, 1345 (Fed. Cir. 2003) ("Thus, a claim reciting 'a widget comprising A and B,' for example, would be infringed by any widget containing A and B, no matter that C, D, or E might be present."). Mylan points to no authority to the contrary, nor to any authority that would persuade the Court to limit the construction of "comprises" based on Claim 1's preamble.

In sum, the Court construes "comprises" to allow for additional unrecited method steps to be performed including the co-administration of other therapies for Parkinson's disease.

D. "in an amount relative to the amount of"

The parties dispute the construction of this term, which appears in Claim 17. The parties' proposed constructions are:

	Teva's Construction	**Orchid's/Watson's/ Apotex's Construction**	**Orchid's/Watson's/ Apotex's Alternate Proposed Construction***
in an amount relative to the amount of	adjusting the amount of Levodopa otherwise administered in light of the subject's response to the amount of R(+)-PAI co-administered with Levodopa.	cannot understand the meaning of this phrase, because it is indefinite	both R(+)-N-propargyl-1-aminoindan and L-Dopa are taken together

* Mylan argues that this claim term does not require construction

Teva argues that a POSA would have recognized, based on the specification and his or her general knowledge of Parkinson's disease, that administering both L-Dopa and a MAO-B inhibitor such as R(+)-PAI to patients would allow the physician to lower the dose of L-Dopa based on the individual patient's response to the combined treatment. Defendants argue in the first instance that the phrase would not have been understood by a POSA. Defendants alternatively argue that R(+)-PAI and L-Dopa must be "taken together."

As an initial matter, the Court declines to find the disputed term indefinite. The Federal Circuit has explained that "[c]laims need not be plain on their face in order to avoid condemnation for indefiniteness; rather, claims must only be *amenable* to construction." Wellman, Inc. v. Eastman Chem. Co., 642 F.3d 1355 (Fed. Cir. 2011) (citation omitted) (emphasis added). "[B]ecause claim construction frequently poses difficult questions over which reasonable minds may disagree, proof of indefiniteness must meet 'an exacting standard.'" Haemonetics Corp. v. Baxter Healthcare Corp., 607 F.3d 776, 783 (Fed. Cir. 2010). Thus, "[a]n accused infringer must . . . demonstrate by clear and convincing evidence that one of ordinary

skill in the relevant art could not discern the boundaries of the claim based on the claim language, the specification, the prosecution history, and the knowledge in the relevant art." Id. "By finding claims indefinite only if reasonable efforts at claim construction prove futile, we accord respect to the statutory presumption of patent validity . . . and we protect the inventive contribution of patentees, even when the drafting of their patents has been less than ideal." Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375 (Fed. Cir. 2001) (citation omitted). Because the term at issue is amenable to construction, the Court does not find the claim indefinite.

The Court further finds that the specification of the '446 Patent supports Teva's construction. As explained above, the specification explains that long-term treatment of Parkinson's disease with L-Dopa had drawbacks, including diminished response over time and adverse side effects. ('446 Patent, 1:35-38; 50-65.) "In order to overcome the drawbacks of L-Dopa treatment, various treatments have been devised in which L-Dopa is combined with MAO inhibitors, with the aim of reducing the metabolic breakdown of the newly formed dopamine." (Id., 1:66-2:3) "One of these selective MAO-B inhibitors, (-)-deprenyl, has been extensively studied and has been used as an MAO-B inhibitor to augment L-Dopa treatment." (Id. 2:25-27.) The addition of (-)-deprenyl to L-Dopa treatment "leads to improvements in akinesia and overall functional capacity as well as the elimination of 'on-off' type fluctuations." (Id. 2:31-37.) Importantly, the specification explains that combining a MAO-B inhibitor with L-Dopa allowed for reduction of the L-Dopa dosage. (See id. 2:38-40) ("Thus, (-)-deprenyl enhances and prolongs the effect of L-Dopa and permits a lowering of the dosage of L-Dopa whereby the adverse effects of L-Dopa treatment are limited.")

Based on this description and his or her general knowledge of treatment of the disease, a POSA would have known the problems associated with long-term L-Dopa treatment. A POSA would also have understood that administration of R(+)-PAI – a MAO-B inhibitor – as an adjunct therapy with L-Dopa for treatment of Parkinson's disease would allow the treating physician to reduce the dosage of L-Dopa. Finally, a POSA familiar with Parkinson's disease would have known that medication dosages would be individualized to the patient based on his or her specific reaction to the combination treatment. (Ruffolo Decl. ¶¶ 82, 83. 86.) In other words, a POSA would understand that patients receiving a combination of R(+)-PAI and L-Dopa treatment would necessarily receive an individualized treatment plan, rather than a standardized one. (Id.)

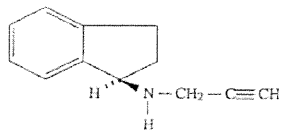
In support of their alternate construction, the Majority Defendants cite to example 18 in the '446 Patent, which provides a sample tablet composition consisting of, inter alia, 5.0 mg of R(+)-PAI and 100.00 mg of L-Dopa. ('446 Patent, example 18.) However, the Federal Circuit has repeatedly cautioned against confining claims to a particular embodiment or importing limitations from the specification into the claims. See Phillips, 415 F.3d at 1323. This is because "[g]enerally, a claim is not limited to the embodiments described in the specification unless the patentee has demonstrated a *clear* intention to so limit the claim's scope." i4i Ltd. P'ship v. Microsoft Corp., 598 F.3d 831, 843 (Fed. Cir. 2010) (emphasis added); see also Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898 (Fed. Cir. 2004) (explaining that "this court has expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment"). Here, the patentees have not expressed "a clear intention" to limit Claim 17 to require that R(+)-PAI and L-Dopa be

"taken together." As such, the Court declines to adopt this narrow construction.

In sum, the Court construes "in an amount relative to the amount of" to mean "adjusting the amount of Levodopa otherwise administered in light of the subject's response to the amount of R(+)-PAI co-administered with Levodopa."

Conclusion

The Court, in accordance with the discussion above, has construed the disputed terms of the '446 Patent. The constructions are as follows:

R(+)-N-propargyl-1- aminoindan	A compound containing the optically active enantiomer rotating plane-polarized light in a clockwise direction and having an R absolute stereochemical configuration of the following chemical structure:  The compound is now known as rasagiline. It is at least substantially pure and may include small amounts of the other enantiomer.
treating a subject for Parkinson's disease…effective to treat the subject	effecting some alleviation in one or more of the symptoms of Parkinson's disease
comprises	allows additional unrecited method steps to be performed including the administration of other therapies for Parkinson's disease
in an amount relative to the amount of	adjusting the amount of Levodopa otherwise co-administered in light of the subject's response to the amount of R(+)-PAI co-administered with Levodopa.

Dated: April 12, 2013

HON. CLAIRE C. CECCHI
United States District Judge